advancing pharmacy solutions
necc

697 Waverly Street, Framingham, MA 01702
Tel: 800.994.6322 or 508.820.0606
Fax: 888.820.0583 or 508.820.1616
www.neccrx.com

General Overview of Policies & Procedures for Compounding Sterile Products

NECC operates in accordance with the following general guidelines when compounding sterile products:

A. Facility/Equipment

a. ISO-5 & ISO-6 Cleanroom(s).
b. Class 10 Microenvironments (barrier isolator).
c. Certified by Massachusetts Board of Pharmacy as a pharmacy with a central venous admixture service (CIVAS) in accordance with Board regulations, 247 CMR 6.01 (6)(c).

B. Monitoring & Maintenance

Comprehensive environmental monitoring program
a. All cleanroom space, air, surfaces and hoods are sampled on a weekly basis, exceeding USP 797.

C. Personnel

a. All sterile compounding is performed by properly trained and validated registered pharmacists.
b. Pharmacy personnel are trained/validated by an outside agency, Professional Compounding Centers of America (PCCA).
c. Personnel are validated on a quarterly basis.

D. Quality Assurance/Quality Control

a. USP Chemicals are obtained only from FDA registered facilities.
b. Formulations are sterilized by 0.22 micron filtration or by autoclaving.
c. Samples from final product batch lots are sent to an independent FDA registered analytical lab for sterility, endotoxin (pyrogenicity) and potency testing.
d. Tested medication is quarantined and dispensed only after the sample has tested negative for endotoxin and microbial contamination.

e. The Quality Assurance Team (QAT), made up of employees from all departments within NECC, meets regularly to review all quality related items.
f. NECC maintains strict environmental testing protocols. Results of these tests are reported via Quarterly QA Reports.
g. All sterile compounding actions are performed in compliance with NECC's Standard Operating Procedures (SOPs). These SOPs have been "mapped" against USP 797 "Pharmaceutical Compounding – sterile preparations" to ensure that all USP 797 requirements are observed.

E. Use-by Dating

Each dosage form is labeled with a BUD/expiration date appropriate to the formulation obtained from:

a. Current literature.
b. Independent stability assay.

F. Packaging

a. Compounded preparations are packaged in containers meeting USP standards.
b. Container used depends on the physical and chemical properties of the compounded preparation.

G. Dispensing

There must be a specific practitioner-patient-pharmacist relationship in place to dispense to an individual patient or facility.

H. Shipping

Medications are shipped overnight (usually via FedEx) in an appropriate container to ensure controlled temperatures and product integrity.

I. Licensing

NECC has undertaken a rigorous licensure process thus giving us the ability to legally dispense prescription medication in all 50 states.

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COMMITMENT TO QUALITY

All Formulations are:

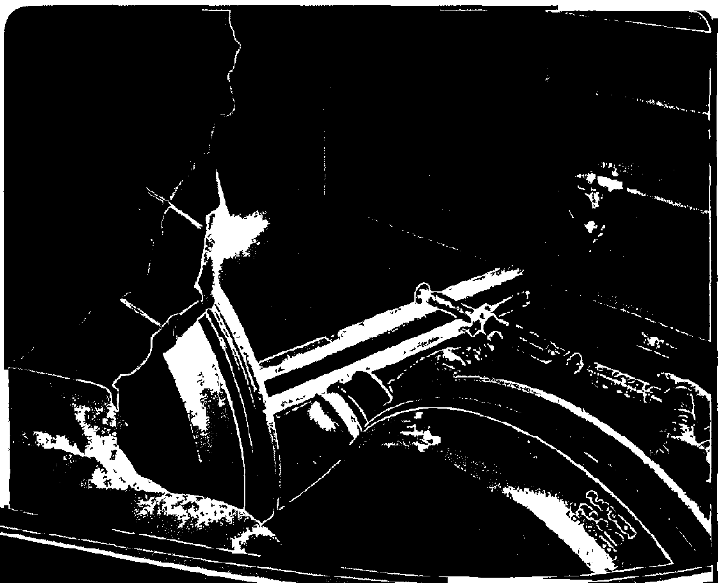
USP 797 Compliant

Strictly Enforced Environmental Monitoring Program

Comprehensive End-Product Testing Program

(Independent Analytical Laboratory Used for ALL End-Product Testing)

- Sterility Testing
- Endotoxin Testing
- Quantitative Testing
- Extended Stability Testing



NECC (New England Compounding Center) is a compounding-only pharmacy dedicated to providing the highest quality compounded medications and services to patients and prescribers. NECC is USP Chapter 797 compliant. Pharmacists formulate all medications with only the highest grade chemicals in a state-of-the-art compounding facility.

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Summary of USP* 797 – Pharmaceutical Compounding – Sterile Preparations

Source of base information – Pharmacopeial Form – Vol 29 (4) July – Aug. 2003

Effective date – January 1, 2004 FDA enforceable

Scope – " The content of this chapter applies to health care institutions, pharmacies, physicians practice facilities and other facilities in which compounded sterile preparations are prepared, stored and dispensed. "

Facilities Impacted by USP 797

1. Facilities in which sterile products are prepared according to the manufacturers' labeling and where manipulations are performed during the compounding of sterile products which increase the potential for microbial contamination of the end product.

2. Facilities where products are compounded using devices or ingredients which are not sterile to prepare products which must be sterilized prior to use.

3. Products may be biologics, diagnostics, drugs, nutrients or radiopharmaceuticals which include, but are not limited to, baths and soaks for live organs and tissues, implants, inhalations, injections, irrigations, metered sprays, ophthalmic and otic preparations.

Microbial Contamination Risk levels

Low Risk Conditions

Compounding with aseptic manipulations entirely with ISO Class 5 or better air quality using only sterile ingredients, products, components and devices

Examples –

A. Using sterile needles and syringes to transfer sterile drugs from the manufacturer's original packaging (vials, ampoules)

B. Manually measuring and mixing no more than three sterile products to compound drug admixtures and nutritional solutions.

Medium Risk Conditions

Multiple individual or small doses of sterile products are compounded or pooled to prepare a compounded sterile product that will be administrated either to multiple patients or to one patient on multiple occasions.

The compounding process includes complex aseptic manipulations other than the single volume transfer.

The compounding process requires an unusually long duration, such as that required to complete dissolution or homogeneous mixing.

The compounded sterile products do not contain broad spectrum bacteriostatic substances and they are administered over several days

For a medium risk preparation in the absence of passing a sterility test, the storage period cannot exceed the following time periods; 30 hours at room temperature, 7 days at cold temperature and 45 days in a solid frozen state at –20 C or colder.
Examples –

A. TPN fluids compounded using manual or automated devices requiring multiple injections, detachments and attachments of the nutrient source products to the device or machine to deliver all nutritional components to the final sterile container.
B. Filling of reservoirs of injection and infusion devices with multiple sterile drug products and evacuations of air from these reservoirs before the filled device is dispensed.
C. Filling of reservoirs of injection and infusion devices with volumes of sterile drug solutions that will be administered over several days at ambient temperatures between 25 and 40 degrees.
D. Transfer of multiple ampoules or vials into a single final sterile container or product.

High

Non-sterile ingredients including manufacturered products for routes of administration other than those listed under c in the introduction are incorporated or a non-sterile device is employed before terminal sterilization.

Sterile ingredients, components, devices and mixtures are exposed to air quality inferior to ISO Class 5. This includes storage in environments inferior to ISO Class 5 of opened or partially used packages of manufactured sterile products that lack antimicrobial preservatives

Non-sterile products are exposed to air quality inferior to ISO Class 5 for at least 6 hours before before sterilization

For high risk preparations in the absence of passing a sterility test the storage periods cannot exceed the following; 24 hours at controlled room conditions, 3 days at cold temperatures and 45 days for solid frozen state at –20 C or colder.

Examples-

A. Dissolving non-sterile bulk drug and nutrient powders to make solution, which will be terminally sterilized.
B. Sterile ingredients, components, devices and mixtures are exposed to air quality inferior to ISO Class 5. This includes storage in environment inferior to ISO Class 5 of opened or partially used packages of manufactured sterile products that lack antimicrobial preservatives
C. Measuring and mixing sterile ingredients in non-sterile devices before sterilization is preformed.

Personnel Training and Evaluation in Aseptic Manipulations Skills

Personnel who prepare compounded sterile products must be provided with appropriate training from expert personnel, audio-video instructional sources, or professional sources before beginning to prepare products.

Personnel shall perform didactic review, written testing, media fill testing of aseptic manipulative shills initially and at least annually for low and medium risk levels and semi annually for high risk level compounding.

Media fill challenge testing will be used to access the quality of aseptic skills.

Clean Rooms

Low and medium risk

Must have an ante area but need not be separated with a physical wall.

Air classification or quality must meet ISO class 8 standards
Class 100,000
Positive pressure to adjacent areas per ISO 14644-4

Physical characteristics of construction:

Walls, floors, fixtures and ceilings should be smooth, impervious and free of cracks, crevices and non-shedding.

Surfaces should be resistant to damage from sanitizing agents.

Junctures of ceilings to walls should be coved and caulked.

If ceilings consist of inlaid panels, the panels should be impregnated with a polymer to render them impervious and hydrophobic and they should be caulked around each perimeter to seal them to the support frame.

Walls may be panels locked together and sealed or epoxy coated gypsum board.

Floors should be overlaid with wide sheet vinyl flooring with heat-sealed seams and coving at the sidewall.

The buffer or ante area should contain no sinks or floor drains.

Gowning

Before entering the ante or buffer area personnel should remove outer lab coats, make-up, jewelry and thoroughly scrub hands and arms to the elbow.

After drying hands and arms they should don clean non-shedding uniforms consisting of:
Hair covers
Shoe covers
Coveralls or knee length coats (coats to fit snugly at the wrists and be zipped or snapped in the front)
Appropriate gloves
Facemasks should be put on after entering the clean room

Leaving and reentry

Upon leaving the clean room the coveralls or coat should be carefully removed and hung outside the entry in the buffer area. Coveralls and coats can only be using for one shift. All other coverings are to be discarded and new ones donned prior to reentry.

Reentry follows original gowning procedure.

High risk

All of low to medium risk procedures and facilities except the ante area must be a separate room

Barrier Isolator (MIC)

A well-designed barrier isolator is an alternative to an ISO class 5 (class 100) LAFW device in an ISO class 8 clean room. The barrier isolator should be supported by adequate procedures for operation, maintenance, monitoring and control.

Physical facility

It is not necessary to locate the barrier isolator in a ISO class 8 area.

Gowning

- Hair covers
- Shoe covers
- Lab coats
- Facemasks (for covering facial hair)

Quality Assurance Program

Must have a formal audit program

- Formalized in writing
- Consider all aspects of preparation and dispensing
- Description of specific monitoring and evaluation activities
- Specifications on how results are to be reported and evaluated
- Identifications of appropriate follow-up mechanisms when action limits or thresholds are exceeded
- Delineation of the individual responsible for each aspect of the QA program.

Validation Minimum Requirements

Low to Medium Risk

Personnel validation – Three consecutive media fill runs without contamination

Revalidation - One media fill run quarterly without contamination

Failure of revalidation – Three consecutive media fill runs without contamination

High Risk

Personnel validation – Three consecutive media fill runs without contamination

Revalidation - One media fill run quarterly without contamination

Failure of revalidation – Three consecutive media fill runs without contamination

Process validation –Three consecutive media fill runs without contamination

Revalidation - One media fill run annually without contamination

Failure of revalidation – Three consecutive media fill runs without contamination

Cleaning and sanitizing the workspaces

Written procedures

At the beginning of each shift

Environmental Monitoring

Verification of sterile compounding equipment

Written plan and schedule for monitoring airborne organisms

Verification of particulate

Verification of viable microorganisms

Verification of automated compounding devices for nutrition compounding

Sterility testing

All high risk compounded sterile products

Administered by injection into vascular and central nervous systems that are prepared in groups of 25 identical or single dose packages or in multi-dose vials for administration in multiple patients.

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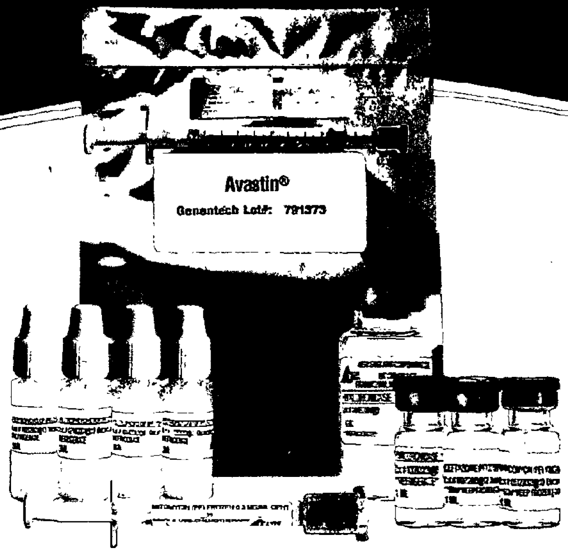

OPHTHALMOLOGY
CUSTOM MEDICATIONS

"Pre-Cataract" Dilation Drops **(Preservative-Free)**	(PE) Phenylephrine (T) Tropicamide (C) Cyclopentolate (K) Ketorolac
	#1) PE-T-C 2.5%-1%-1% #2) PE-T-C 10%-1%-1% #3) PE-T-C-K 2.5%-1%-1%-0.5% #4) PE-T-C-K 10%-1%-1%-0.5%
Avastin™ - "Unit-Dose Syringe"	1.25mg/0.05mL Syringe/ Needle/ Tamper-Evident, Light-Resistant Mylar Bag
Triamcinolone Acetonide	40mg/mL (PF), 1mL Vial
Frozen/Unit-Dose Antibiotics	Vancomycin 10mg/mL, 1mL Vial Ceftazidime 22.5mg/mL,1mL Vial
Hyaluronidase	150u/mL, 1mL or 10mL Vial
Mitomycin	0.2-0.5mg/mL, 1mL Volume in a 3mL Syringe, "Frozen" Unit of Use

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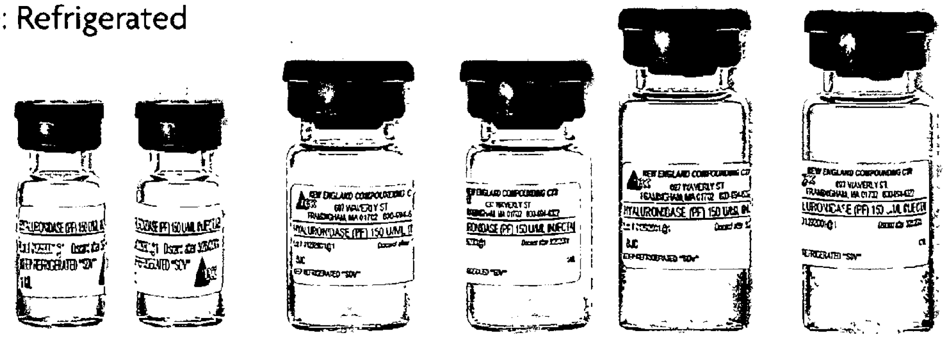
Hyaluronidase Preservative-Free

- 150u/mL Preservative-Free
- Provided in a 1mL, 5mL or 10mL Sterile Vial
- Beyond Use Date: 180 Days
- Storage: Refrigerated



All CSP Formulations are:

- USP 797 Compliant
- Compounded for your patients by pharmacists extensively trained in aseptic compounding
- Prepared in a Class 10 Microenvironment (barrier isolator)
- Comprised of USP quality ingredients

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Hyaluronidase

Description and Common Uses:

1. Hyaluronidase: a preparation of purified bovine (cow/bull) testicular hyaluronidase. Dispensed as a sterile, colorless solution. It modifies the permeability of connective tissue through hydrolysis of *hyaluronic acid.* It temporarily decreases the viscosity of cellular cement and promotes diffusion of injected fluids thus facilitating their absorption. It is used as an adjunct to increase the absorption and dispersion of other injected drugs...usually local anesthetics such as *Lidocaine.*

    A. Mixed with Lidocaine (150units per 10ml of 1% Lidocaine) and injected behind/around the orbit of the eye prior to cataract surgery to enhance the absorption of Lidocaine into and around the muscles that control the movement of the eye in the socket. This is called a "retro-bulbar injection/block". Necessary to prevent movement of eye during cataract surgery. If Hyaluronidase is not mixed with the Lidocaine then there is the risk of an incomplete block and potential for movement of eye in socket during surgery.

    B. Mixed with Lidocaine by plastic surgeons to enhance dispersion of the drug when injected into face prior to facial plastics procedures. Ultimately used to produce "better"/ more complete anesthesia.

    C. Pain management: can be used as a preservative-free product during "Racz procedure"= injected into areas of epidural space to promote dissolution of Hyaluronic acid component of scar tissue that may be impinging on nerve roots and causing pain.

Retro Bulbar Blocks

Lidocaine in Various Concentrations (mg/mL or %)

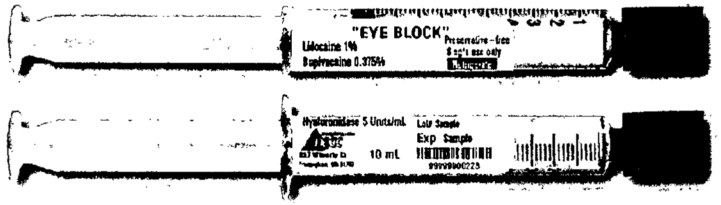
Bupivacaine in Various Concentrations (mg/mL or %)

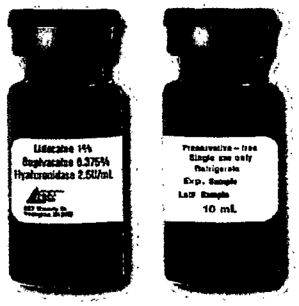
- **Hyaluronidase in Various Concentrations (Units or mL)**

- Available in Various Concentrations (Custom per Facility)

  Provided in a Luer-lock Syringe with a Tamper Evident Cap and

  Various Vial Sizes
- Beyond Use Dating: Varies, Based on Final Formulation





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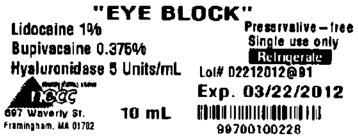
ANALYTICAL RESEARCH LABORATORIES
840 RESEARCH PARKWAY, SUITE 546
OKLAHOMA CITY, OK 73104
PHONE (405) 271-1144
FAX (405) 271-1174

Certificate Of Analysis

CLIENT: New England Compounding Center-MA



"EYE BLOCK"
Lidocaine 1%
Bupivacaine 0.375%
Hyaluronidase 5 Units/mL
Preservative-free
Single use only
Refrigerate
Lot# 02212012@91
Exp. 03/22/2012
NECC
697 Waverly St.
Framingham, MA 01702
10 mL
99700100228

ARL #: 171267-01
LOT #: 02212012@91
DESCRIPTION: Lidocaine 1%/Bupivacaine 0.375% (PF) Eye Block
DATE RECEIVED: 03/15/2012 25 Day
STORAGE: 2°C to 8°C (35.6°F to 46.4°F)
CONTAINER: One 10 mL syringe

Analyte / Specifications	Expected Amount	Units	Results	% Of EXP.	Test Method	Date Tested
Lidocaine HCl Specifications = 90% - 110%	1.0	%	0.233	23.3%	HPLC	3/19/2012
Bupivacaine HCl Specifications = 90% - 115%	0.375	%	0.384	102.4%	HPLC	3/19/2012
Lidocaine HCl Rerun Specifications = 90% - 110%	1.0	%	0.238	23.8%	HPLC	3/19/2012
Lidocaine HCl Average Specifications = 90% - 110%	1.0	%	0.235	23.5%	HPLC	3/19/2012

alex tang - Laboratory Supervisor

03/19/2012
Date Reported

ARL Form QUF-078-V4 03/05/2010

Mass Eye Ear. exp 3/22/2012
please print an actual label for this lot# that would have been on syringe.

Results reported above relate only to the sample that was tested.

Page 1 of 1

New England Compounding Center, Inc.
PO Box 4146
Woburn, MA 01888-4146
Ph. 508-820-0606
Fx. 508-820-1616

Credit Memo

Date	Credit No.
3/27/2012	210066

Customer
MASSACHUSETTS EYE AND EAR INFIRMARY PO Box 9684 Manchester, NH 03108

P.O. No.	Rep	Project
	BM	

Description	Qty	Rate	Amount
LIDOCAINE/BUPIVACAINE/HYALURONIDASE (PF) 1%/0.375%/5U/ML INJECTABLE, 10 ML CONTROL SYRINGE	-300	10.00	-3,000.00
	-3	30.00	-90.00
AE12007 - credit for product sent on 02/22/2012			

Total	$-3,090.00
Invoices	$0.00
Balance Credit	$-3,090.00